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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/511,008	02/22/2000	Gregory S. Hageman	20618-000600US	3115

7590 10/06/2003

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/511,008	HAGEMAN, GREGORY S.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10,21 and 68-79* is/are pending in the application.

4a) Of the above claim(s) *10,21,70-72 and 74-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,68,69,73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, drawn to a method for assessing a subject's risk for an aortic aneurysm with a drusen-associated *dendritic cell* protein marker and species election of CD1a, in Paper No. 22 is acknowledged. The traversal is on the ground(s) that restricting a single claim into multiple inventions is directly contrary to controlling law, and that a search of all four groups can be made without serious burden. This is not found persuasive for reasons of following. The cited C.C.P.A. decision indicates that applicant has the right to have each claim examined on the merits, it is improper if a single claim is required to be divided up and certain claims or the full scope of the claim would never be considered on the merits when the totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. This is not the case for the instant restriction, wherein the totality of the base claim has not been affected by the division of a single claim into four groups of inventions, i.e. each of the claims would be examined eventually when all four groups of inventions are examined. Accordingly, such action would not affect the rights of the applicant eventually to have each of the claimed invention examined in the form he considers to best define his invention. Therefore, the restriction is proper. With respect to the search burden, although the four groups have the same classification, i.e. they are all drawn to a method for assessing a subject's risk for an aortic aneurysm with a protein marker. The recited markers embrace considerably divergent subject matter,

and would require distinct search criteria and technical consideration as explained in the previous Office action (paper #20, pages 3-4), and as evidenced by the prosecution history. Thus, examining four groups of the invention together in this application would place a serious search burden on the Office. M.P.E.P. states, "FOR PURPOSES OF THE INITIAL REQUIREMENT, A SERIOUS BURDEN ON THE EXAMINER MAY BE PRIMA FACIE SHOWN IF THE EXAMINER SHOWS BY APPROPRIATE EXPLANATION OF SEPARATE CLASSIFICATION, OR SEPARATE STATUS IN THE ART, OR A DIFFERENT FIELD OF SEARCH AS DEFINED IN MPEP § 808.02". Therefore, it is maintained that these inventions are distinct due to their divergent subject matter. Further search of these inventions is not co-extensive. The requirement is still deemed proper and is therefore made **FINAL**.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-6, 10, 21, 68-79 are pending, however, claims 10, 21, 70-72, 74-79 are withdrawn from further consideration by the Examiner, pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim. Claims 1-6, 68, 69, and 73 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated.

Claim Objections

Claims 1 and 68 are objected to because of the following informalities: they encompass more than one invention as defined in Paper #20, upon election of an invention for examination, said claim should be amended so that it only reads upon the elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 68, 69, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-6, 68, 69, and 73 are rejected under 35 U.S.C. 112 first paragraph, because the specification as originally filed does not describe the invention as now claimed. The original disclosure fails to specify a method for detecting the CD1a levels in a blood, plasma, serum or urine sample of patients suffering either macular degeneration or aortic aneurysm as now claimed. The claimed method is now considered to be new matter.

To the extent that the claimed method is not described in the instant disclosure, claims 1-6, 68, 69, 73 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

MPEP 2163.02 teaches that "WHENEVER THE ISSUE ARISES, THE FUNDAMENTAL FACTUAL INQUIRY IS WHETHER A CLAIM DEFINES AN INVENTION THAT IS CLEARLY CONVEYED TO THOSE SKILLED IN THE ART AT THE TIME THE APPLICATION WAS FILED...IF A CLAIM IS AMENDED TO INCLUDE SUBJECT MATTER, LIMITATIONS, OR TERMINOLOGY NOT PRESENT IN THE APPLICATION AS FILED, INVOLVING A DEPARTURE FROM, ADDITION TO, OR DELETION FROM THE DISCLOSURE OF THE APPLICATION AS FILED, THE EXAMINER SHOULD CONCLUDE THAT THE CLAIMED SUBJECT MATTER IS NOT DESCRIBED IN THAT APPLICATION". In the instant case, the specification as originally filed describes that drusen cores are present in approximately 40% of drusen, that drusen cores, and the cells from which they are derived, are strongly reactive with CD1a and other CD markers that associated with dendritic cells, that the immunophenotyping data when combined with ultrastructural analyses, provide strong evidence that drusen cores are derived from choroidal dendritic cells (Specification, Example 7). However, the specification is completely silent with respect to the levels of CD1a in biological samples of blood, serum, or urine nor how they are changed in disease. Thus, the amendment is a departure from or an addition to the disclosure of the application as originally filed, accordingly, it introduces new matter into the disclosure.

For reasons set forth above, the amendment filed 3/6/03 is objected to under 35 U.S.C. §132 because it introduces new matter into the disclosure. 35 U.S.C. §132 states that no amendment shall introduce new matter into the disclosure of the invention. Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-6, 68, 69, and 73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether the disclosure satisfies the enablement requirements and whether undue experimentation would be required to make and use the claimed invention are summarized in *In re Wands*, (858 F2d 731, 737, 8 USPQ 2d 1400, 1404, (Fed Cir.1988)). These factors include but are not limited to the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, the breadth of the claims, and amount of direction provided. The factors most relevant to this rejection are the scope of the claims relative to the state of the art and the levels of the skilled in the art, and whether sufficient amount of direction or guidance are provided in the specification to enable one of skill in the art to practice the claimed invention.

The previous rejection under this section has been withdrawn in view of the amendment. Particularly, the amended claims are now drawn to a method for assessing a subject's risk for aortic aneurysm, rather than diagnosis; and the proteins subject to be detected have changed. Upon search and consideration, new grounds of rejections are necessitated and appear below.

The amended claims are drawn to a method comprising detecting one or more protein markers for macular degeneration in a blood, plasma, serum, or urine sample from a subject to be evaluated, and the elected species of a protein marker is drusen-associated dendritic cell marker, CD1a. The specification teaches that drusen cores are present in approximately 40% of drusen, that drusen cores, and the cells from which they are derived, are strongly reactive with CD1a and other CD markers that associated with dendritic cells, that the immunophenotyping data when combined with ultrastructural analyses, provide strong evidence that drusen cores are derived from choroidal dendritic cells (Specification, Example 7). However, the specification is completely silent with respect to the levels of CD1a in biological samples of blood, serum, or urine nor how they are changed in diseases, such as AA or AMD.

Turning to the knowledge of the skilled in the art, it is well known in the art that CD1a-d are highly specific markers for human Langerhans cells and expressed on the surface of dendritic cells (Pubmed, and Davison college datasheet, 2003). It is also well known in the art that dendritic cell are involved in the pathology of aortic aneurysm. For example, *Bobrysev et al* (Cardiovas Surg 1998;6:240-9, IDS/AI) teach CD1a is detectable in the aneurysm wall and co-existent with T cells (§ Results). However, the

prior and post-filing art of record are silent with regard to whether CD1a is detectable in biological samples, such as blood, serum, or urine, and it is not known how the marker may change under disease condition in these samples.

The claims call for comparing the level of the protein markers of the test population to that of the control population, however, in light of the teachings in the art, it appears that the biological localization of CD1a is bound to cell membrane and cytosol, and is unlikely to be detected in the biological samples of serum or urine, and it is unlikely that CD1a would detectably different in the blood sample of the two populations. For example, *Van der Well et al* (Mole Biol Cell 2003;143378-88) teach the intra-cellular trafficking of CD1 isoforms during dendritic cell maturation using electron microscopy, flow cytometry, and endocytosis assays. *Van der Well et al* teach that CD1a is expressed abundantly on the plasma membrane and in early recycling endosomes (left column, page 3379), that CD1 cell surface expression was *not* detectably up-regulated during or after dendritic cell maturation, and the changes occurred in sub-cellular trafficking of CD1 molecules, particularly CD1b and CD1c (left column, page 3387), while CD1a expression *remained* restricted to the plasma membrane and early endocytic tubulovescular structures. In view of such, the invention does not appear to be enabled in the absence of clarification of the contradictory evidence found in the references.

Moreover, macular degeneration or aortic aneurysm are localized pathological alterations, neither the prior art of record nor the specification teaches how the localized change of dendritic cells correlates with the total number or maturity of dendritic cells in

the circulation (blood), quantitative levels of dendritic cell markers in the biological samples, or any detectable change in disease, and whether techniques such as immunostaining, western blot or ELISA can sufficiently detect such change. Accordingly, the specification fails to provide an enabling disclosure to teach how to assess the risk of aortic aneurysm via detecting protein markers such as CD1a in blood, plasma, serum or urine samples. It would have required undue experimentation for the skilled artisan intending to practice the instant invention.

The claimed method comprises a step of selecting a control population that "does not have the aortic aneurysm", the specification fails to teach how to reasonably determine whether an individual has aortic aneurysm since this could not be readily determined due to the anatomical location of aortic aneurysm. More importantly, since the goal of the method is to evaluate the risk of having aortic aneurysm, it is illogical to have a method step that involves determining the presence or absence of the aortic aneurysm as a pre-requisite for practicing the method. In view of such, it would have required undue experimentation for the skilled artisan intending to practice the instant invention.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is now claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 68, 69, and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite because of the claim recitation, "the control population comprises at least one individual", which encompasses one individual. However, given the plain meaning of the phrase, one individual could not be categorized as "a population".

The claims are vague and indefinite because the preamble of the claim is for assessing the risk of having aortic aneurysm in a subject, yet the method step requires determination of the absence of aortic aneurysm. The goal of the method is inconsistent with the method steps because if the aortic aneurysm could be readily determined, what is the purpose of assessing the risk factor?

Citation of Pertinent Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Bobrysev et al, Cardiovas Surg 1998;6:240-9, IDS/AI.

Koch et al, Am J Pathol 1990;137:1199-1213, IDS/BI.

Pearce et al, Annals NY Acad Sci 1996 ;800 :175-85.

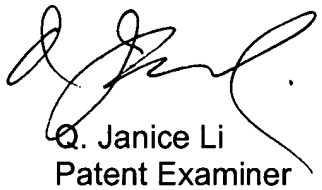
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).



Q. Janice Li
Patent Examiner
Art Unit 1632

QJL
September 30, 2003